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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

16 FEB 2005

Applicant's or agent's file reference 3-32620A	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/09302	International filing date *(day/month/year)* 21.08.2003	Priority date *(day/month/year)* 22.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K47/00		
Applicant NOVARTIS CONSUMER HEALTH S.A. et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.02.2004	12.11.2004
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer von Eggelkraut-Gotta Telephone No. +31 70 340-4732

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/09302

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-9	as originally filed

Claims, Numbers

1, 2	as originally filed
3 (part), 4-16	received on 11.08.2004 with letter of 11.08.2004

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-16
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-16
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-16
	No:	Claims	

2. Citations and explanations

see separate sheet

V. Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

D1: WO 02/078648 A (LARNIER CATHERINE ;NOVARTIS CONSUMER HEALTH SA (CH); STEIGER MICHE) 10 October 2002 (2002-10-10)
D2: US-A-4 917 886 (ASCHE HENNING ET AL) 17 April 1990 (1990-04-17)
D3: US-A-5 350 769 (IKEDA YASUO ET AL) 27 September 1994 (1994-09-27)

D1 is published after the valid priority date of the present application and is not relevant for question of novelty or inventive step.

2 **NOVELTY** (Art. 33(2) PCT)

2.1 In view of the prior cited, claims 1-16 appear to be novel and meet therefore the requirements of Art. 33(2) PCT.

2.2 Document D2 discloses cream compositions comprising 1% diclofenac sodium. A lipid and a surfactant are not disclosed (page 2, line 60 - page 7, line 7).

2.3 Document D3 discloses diclofenac emulsion-gels with diethanolamine, but without a basic agent selected from ammonia, sodium hydroxide and potassium hydroxide. The diclofenac content is to high (examples 1, 2).

3 **INVENTIVE STEP** (Art. 33(3) PCT)

3.1 The document D3 is regarded as being the closest prior art to the subject-matter of claims 1, 3 and 5, and shows diclofenac emulsion-gels. The subject-matter of claims 1,3 and 5 differs from these known compositions in that no organic amine such as diethanolamine is present but a basic agent selected from ammonia, sodium hydroxide

and potassium hydroxide are present. The amount of diclofenac sodium is 0.02-0.4% (w/w) and therefore lower than in D3.

3.2. The technical effect is the absence of organic amines in the composition and consequently of nitrosamines, as well as an emulsion-gel comprising no diclofenac particles.

3.3 The problem to be solved by the present invention may be regarded as the provision of diclofenac compositions achieving similar effects as known diclofenac compositions but comprising less diclofenac, providing reproducible permeation through the skin and being free of organic amines.

3.4 The solution to this problem proposed in claims 1, 3 and 5 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons: The prior art does neither disclose nor suggest an emulsion gel consisting essentially of the compounds recited in claims 1, 3 and 5, including a diclofenac sodium content of 0.02-0.04% (w/w) and a basic substance selected from ammonia, sodium hydroxide and potassium hydroxide.

3.5 Claims 2,4,6-16 are dependent on claims 1,3 and 5 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

4 Certain defects

4.1 Although claims 1,3 and 5 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought and in respect of the terminology used for the features of that subject-matter. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

(e) 0.2-3% (w/w) of at least one gelling agent selected from the group consisting of carbomers,
(f) 2-8% (w/w) of at least one lipid forming the oily phase of the emulsion-gel,
(g) 1-5% (w/w) of at least one non-ionic surfactant, and
(h) a basic agent selected from the group consisting of ammonia, sodium hydroxide and potassium hydroxide to adjust the pH of the total composition to 6.5-8.

4. A composition according to claim 3, which consists essentially of
(a) 0.05-0.3% of diclofenac sodium salt,
(b) 60-92% of water,
(c) 0-25% of ethanol, isopropanol, or mixtures thereof,
(d) 3-20% of propylene glycol,
(e) 0.3-2% of at least one gelling agent selected from the group consisting of carbomers,
(f) 3-7% of at least one lipid forming the fatty phase of the emulsion-gel,
(g) 1-3% of at least one non-ionic surfactant, and
(h) ammonia to adjust the pH of the total composition to 6.5-8.

5. A pharmaceutical composition intended for topical use, which composition is in the form of an opaque emulsion-gel and which composition consists of
(a) 0.02-0.4% (w/w) of diclofenac sodium salt,
(b) at least 50% (w/w) of water,
(c) 0-30% (w/w) of at least one C2-C4-alkanol,
(d) 3-20% (w/w) of a glycol solvent selected from the group consisting of propylene glycol and polyethylene glycol (200-20000),
(e) 0.2-3% (w/w) of at least one gelling agent selected from the group consisting of carbomers,
(f) 2-8% (w/w) of at least one lipid forming the oily phase of the emulsion-gel,
(g) 1-5% (w/w) of at least one non-ionic surfactant, and
(h) a basic agent selected from the group consisting of ammonia, sodium hydroxide and potassium hydroxide to adjust the pH of the total composition to 6.5-8.

6. A composition according to any one of claims 1, 3 or 5, wherein the polyethylene glycol (200-20000) usable as component (d) is selected from polyethylene glycol (200-1000).

7. A composition according to any one of claims 1-6, which comprises (c) in an amount of from 5 up to 25% and (d) in an amount of from 3 up to 7% of the total composition.

8. A composition according to any one of claims 1-6, which comprises (c) in an amount of from 0 up to 5% and (d) in an amount of from 3 up to 20% of the total composition.

9. A composition according to any one of claims 1-6, which comprises (c) in an amount of from 0 up to 5% and (d) in an amount of from 3 up to 7% of the total composition.

10. A composition according to claim 8 or claim 9, which is devoid of the component (c).

11. A composition according to any one of claims 1-9, which comprises as C2-C4-alkanol (c) isopropanol.

12. A composition according to any one of claims 1-11, which comprises as gelling agent (e) carbomer 980, carbomer 940, carbomer 981, carbomer 941, carbomer 974, carbomer 934, carbomer 910, or a mixture of any of said carbomers.

13. A composition according to any one of claims 1-12, which comprises as lipid (f) either a mixture of paraffin and C6-C12-alkanoic acid C12-C18-alkyl esters, or a mixture of isopropyl myristate and C6-C12-alkanoic acid C12-C18-alkyl esters.

14. A composition according to any one of claims 7-9, which comprises as lipid (f) isopropyl myristate.

15. A composition according to any one of claims 1-14, which comprises as non-ionic surfactant (g) a polyoxyethylene (10 to 30) fatty alcohol ether.

16. A composition according to any one of claims 1-15, which is devoid of a chemical stabilizer.
